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Efficacy of Statins with Ezetimibe and Bempedoic Acid in Achieving Target LDL Levels in Post MI Patients

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Abstract: Dyslipidaemia is a major risk factor in the progression of Myocardial Infarction. So, we need to pay closer attention to achieving desired Lipid levels in MI patients to prevent progression to Congestive Heart Failure. The study was conducted in Cardiology In-Patient and Out-Patient departments after the approval of the Ethical Committee. Patients were selected based on the inclusion and exclusion criteria. Patients were divided into 3 groups. Group 1 served as Control group patients who were treated with Statins. Group 2 patients were treated with Statin+ Ezetimibe and Group 3 patients were treated with Statins + Bempedoic acid. The clinical efficacy of the drugs given in our study period was analysed based on the data collected from Groups 1, 2 and 3. The three therapies-- statin, combination of statin and bempedoic acid, and a combination of statin and ezetimibe were given to the patients who had signed up. The results showed that for a period of three months, Statin + Bempedoic acid therapy and Statin + Ezetimibe combination therapy had better efficacy in achieving target LDL levels in comparison to Statin monotherapy. We conclude that among both combination therapies, Statin + Ezetimibe therapy has shown the most efficacy in achieving target LDL levels in post MI patients.

Keywords: Dyslipidaemia, Myocardial Infarction, Anti-lipidemic drugs, LDL cholesterol, Atherosclerotic cardiovascular diseases

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Introduction

Dyslipidaemia is caused due to the fact of existing of abnormal lipid levels in the blood of an individual. While the name includes various types, the most common types of dyslipidaemia include: Increased levels of LDL, or bad cholesterol; Decreased levels of HDL, or good cholesterol; Increased levels of triglycerides; Increased levels of cholesterol, refer to more triglyceride and LDL levels (Anderson *et al.,* 2016). Lipids, or fats, are the fundamental components of life and they supply energy to the cells for their proper functioning. Lipids consist of:

- LDL-C is known as bad cholesterol because it may lead to plaque formation within the blood carrying vessels.
- HDL-C is considered good cholesterol due to the fact it may help to dispose of LDL-C.
- TGL occur when calories aren't burned properly and instead are saved in fat cells. (Apple *et al.*, 2004).

Healthy lipid levels generally differ from one individual to another. People with high LDL and triglyceride levels, or reduced HDL levels, are more likely to develop atherosclerosis.(Barengo Nc, 2004). Atherosclerosis occurs when solid, oily deposits known as plaque form in vasculature, making blood circulation difficult (Brarks, 2004). Over a long period of time, those plaques will increase in the amount and lead to various circulatory problems, like strokes and cardiac events. (Bhardwaj ss *et al.*, 2007).

Myocardial infarction (MI) is a cardiovascular disorder in which the blood flow to a portion of the heart is stopped, which leads to necrosis of the heart muscle (Dobson, 1996). This generally occurs due to a clot in the epicardial arteries that supply blood to the specified territory of the heart muscle (Fransson *et al.*, 2004). Most myocardial infarctions occur because of underlying coronary artery disease.(fuller *et al.,* 1983). due to coronary artery occlusion, the myocardium suffers from a lack of oxygen (Frangogiannis, 2015). A prolonged shortage of oxygen delivery to the myocardium can result in necrosis and myocardial cell death (Gongj *et at.,* 2013).] Patients can show symptoms of chest pain or stress that may radiate to the neck, jaw, arm, or shoulder. (Janszky and Koshman, 2005). In addition to the previous records and physical exam, myocardial ischemia can be related to ECG modifications and increased biochemical markers like cardiac troponins (Guk and Haffner *et al.*, 1998).

Inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, also known as statins, are a well-known class of medications for the management of hypercholesterolemia but come with potentially catastrophic side effects (such as rhabdomyolysis). The cytochrome P450 system in the liver and the gut is where the lipophilic medications Lovastatin, Simvastatin, Atorvastatin, and Fluvastatin are metabolized, making them susceptible to interact with concurrent administered drugs that are vying for this system's metabolism (Patel, 2003).

Bempedoic acid is a brand-new non-statin LDL-lowering medication that, like statins, targets the liver's cholesterol-production paths. In contrast to statins, which inhibit HMG CoA reductase, bempedoic acid inhibits ATP-citrate lyase (ACL), which is two steps input and output of HMG CoA reductase. (Quintana Ds *et al.,* 2013). Bempedoic acid is supplied as a prodrug and is transformed into an active coenzyme, unlike statins. an enzyme type that is exclusive to the liver and not present in muscles. Bempedoic acid is a possible substitute for people with statin-related muscular complaints because it does not have active metabolites in skeletal muscles (SAMS). Bempedoic acid's impact on cardiovascular death and disease still seems to be unknown (Rossen *et al.,* 1994).

Ezetimibe is a medication that is used to maintain and treat hypercholesterolemia. It belongs to a brand-new class of selective cholesterol-absorption inhibitors (Reimer *et al.,* 1983). It is prescribed to person who are suffering with primary and mixed hyperlipidaemia, familial

Table 1: Descriptive Analysis of Study Group (N=30)

Study Group	Frequency	Percentage
Group 1	10	33.33%
Group 2	10	33.33%
Group 3	10	33.33%

hypercholesterolemia (HoFH), and homozygous sitosterolaemia to lower total cholesterol, LDL, Apo-B and phytosterolaemia. (Stamatakis *et al.,* 2009). This study discusses ezetimibe's indications, actions, and contraindications as valuable drug in the management of hypercholesterolemia (Skolnik, 2017). This study also emphasizes the administration and monitoring principles that the interprofessional team should use to manage patients with hypercholesterolemia who are taking ezetimibe. (Zhu *et al.,* 2014).

Materials and Methods

Participants:

30 patients was included in this study.

Inclusion criteria: (i) Patients with irrespective of gender; (ii) Patients above 18 years old; (iii) Post-MI stable patients within 3 months; and (iv) Post ACS patients.

Exclusion criteria: (i) Post-MI stable patients after 3 months; (ii) Patients with end-stage CKD and Liver damage; (iii) Patients who are not willing to cooperate; (iv) Patients below 18 years old; (v) Pregnant women; and (vi) Patients who are chronic alcoholics.

The study was conducted for a period of 6 months as a Prospective Observational study. Patients are selected based on the inclusion and exclusion criteria. The patient data is collected in a Proforma (Data collection form) during the study period. Patients are divided into 3 groups, Group 1, 2, and 3. Group 1 is Control group patients who are treated with Statins. Group 2 is patients treated with Statins + Ezetimibe. Group 3 patients are treated with Statins + Bempedoic acid. The clinical efficacy of the drugs given in our study period is analysed based on the data collected from Group 1, 2 and 3. A Lipid Profile test was performed between different groups to find out the best way to control lipid levels.

Statistical Analysis:

Lipid profile parameters, Coronary Angiogram finding, and diagnosis were considered as outcome variable. Study group (Group 1, Group 2 and Group 3) was considered as Primary explanatory variable. Age, Gender, etc., were considered as study relevant variables. Descriptive analysis was carried out by frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, cluster bar chart etc. Analysis was carried out using SPSS-21.

Results and Discussion

Table 1 shows that among all the study population, 10 (33.33%) participants were in group 1, 10 (33.33%) were in group 2 and 10 (33.33%) were in group 3.

30 patients were divided into 5 groups where 1 (3.30%) participant was in group 31-40 age, 4 (13.30%) participants were in group of 41-50 age, 7 (23.30%) participants were in group of 51-60 age, 15 (50%) participants were in group of 61-70 age and 3 (10%) participants were in group of 71-80 age (Table 2).

Table 3 shows that among 30 participants, 24 participants were male i.e., 80% and 6 participants were female i.e., 20%.

Table 4 shows that among 30 participants, there was 0 participant in the Underweight

Table 2: Distribution of Patients as per different age groups

Age Group	No. of Participants	Percentage
31-40	1	3.30%
41-50	4	13.30%
51-60	7	23.30%
61-70	15	50%
71-80	3	10%

Table 3: Distribution of Patients According to Gender

Sex	No. of Patient	Percentage
M	24	80%
F	6	20%

Table 4: Distribution of Patients Based on Their BMI

BMI Range	No. of Participants
Underweight (0-18.5)	0
Normal weight (18.5-24.9)	12
Overweight (25-29.9)	14
Obese (30-40)	4

Table 5: Distribution of patients based on their co - morbidities

Comorbidities	No of Patients
HTN	6
T2-DM	4
HTN and DM	12
NIL	8

category, 12 participants in the Normal weight category, 14 participants in the Overweight category and 4 participants in the Obese category.

Out of 30 participants 6 were with Hypertension, 4 with Type 2 Diabetes Mellitus and 12 patients were suffering from both Hypertension and Diabetes and 8 participants were without any Co-morbid conditions (Table 5).

Out of 30 participants, 15 were suffering from Single Vessel Disease, 5 were suffering from Double Vessel Disease and 10 were suffering from Triple Vessel Disease (Table 6).

The baseline and follow up LDL cholesterol with statin therapy of each patient is shown in Table 7. Similarly the baseline and follow up of LDL cholesterol with statin+ bempedoic acid therapy and statin+ ezetimibe therapy are depicted in Table 8 and Table 9, respectively.

Out of the 30 participants, 10 participants who were administered with statins showed 33.50%

Table 6: Comparison of Coronary Angiogram Finding

Coronary Angiogram finding	No. of Participants
Single vessel disease	15
Double vessel disease	5
Triple vessel disease	10

Table 7: Comparison of LDL Cholesterol With Statin Therapy

Participants	Baseline	Follow Up
PATIENT 1	109	79
PATIENT 2	85.6	54
PATIENT 3	89.4	54
PATIENT 4	61	38
PATIENT 5	74	49
PATIENT 6	117	74
PATIENT 7	49	32
PATIENT 8	34	21
PATIENT 9	82	53
PATIENT 10	52	31

Table 8: Comparison of LDL Cholesterol With Statin + Bempedoic Acid Therapy

Patients	Baseline	Follow Up
PATIENT 1	107	60.2
PATIENT 2	148.3	91.46
PATIENT 3	77.6	41.3
PATIENT 4	96	50.6
PATIENT 5	49	25.38
PATIENT 6	48	36.24
PATIENT 7	47	22.2
PATIENT 8	79	41.56
PATIENT 9	87	46.81
PATIENT 10	82.4	43.84

Table 9: Comparison Of LDL Cholesterol With Statin + Ezetimibe Therapy

PATIENTS	BASELINE	FOLLOW UP
PATIENT 1	166	97.3
PATIENT 2	52.4	38.29
PATIENT 3	86	45.58
PATIENT 4	74	48.48
PATIENT 5	139	79.5
PATIENT 6	87	59.37
PATIENT 7	84	49.84
PATIENT 8	72	36.72
PATIENT 9	88	57.52
PATIENT 10	73	37.96

Table 10: Comparison of Percentage reduction of LDL between study groups

PARAMETERS	MEAN		
	Statins	**Statin+Bempedoic Acid**	**Statin+Ezetimibe**
LDL (BASELINE)	75.3	72.13	92.14
LDL (FOLLOW-UP)	48.5	45.95	55.1
Percentage of Reduction	35.50%	36.29%	40.1%

reduction in LDL Cholesterol levels, another 10 participants who were administered with Statin+Bempedoic acid showed 36.29% reduction in LDL Cholesterol levels, and the other 10 participants who were administered with Statin+Ezetimibe showed 40.10% reduction in LDL Cholesterol levels (Table 10).

After a post-MI, it is necessary to keep your lipid profile at a healthy level. We included post-myocardial infarction patients in our studies. The three therapies-- statin, combination of statin and bempedoic acid, and a combination of statin and ezetimibe-- were given to the patients who had signed up. For three months, the patients had meticulous follow-up in order to assess the effects of various therapies on their LDL cholesterol levels from the beginning to the end of the follow-up period. Following the follow-up period, the LDL levels of the patients were measured, and each therapy's percentage of reduction was calculated. As per the study, using statin medication alone, in addition with bempedoic acid, or with ezetimibe results in percentage reductions of LDL levels of 35.5%, 36.29%, and 40.10%, respectively.

As per the data we have gathered, men experienced more myocardial infarctions than women. Also, it indicates that a greater proportion of patients are in the 60–70 year age range. Also, it was observed that more overweight patients were prevalent.

The study also showed that among the individuals having coronary angiograms, 15 had single vessel disease, 5 had double vessel disease, and 10 had triple vessel disease.The results showed that, for a period of three months, Statin +

Bempedoic acid combination therapy and Statin + Ezetimibe combination therapy has shown better efficacy in achieving target LDL levels in comparison to Statin monotherapy. From our observations we have concluded that among both combination therapies, Statin + Ezetimibe therapy has shown the most efficacy in achieving target LDL levels in post MI patients.

Conclusion

The results showed that, for a period of three months, Statin + Bempedoic acid therapy and Statin + Ezetimibe combination therapy has shown better efficacy in achieving target LDL levels in comparison to Statin monotherapy. From our observations we have concluded that among both combination therapies, Statin + Ezetimibe therapy has shown the most efficacy in achieving target LDL levels in post MI patients.

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